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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/726,348	12/01/2000	Ying-Fei Wei	PF220P1	3638

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EXAMINER
SPECTOR, LORRAINE

ART UNIT	PAPER NUMBER
1647	18

DATE MAILED: 01/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	Examiner	Group Art Unit	

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Response

A SHORTENED STATUTORY PERIOD FOR RESPONSE IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a response be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for response specified above is less than thirty (30) days, a response within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for response is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to respond within the set or extended period for response will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 8/16/02 + 11/8/02.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 19, 26-79 is/are pending in the application.

Of the above claim(s) 19 is/are withdrawn from consideration.

☒ Claim(s) 60-67, 76-79 is/are allowed.

☒ Claim(s) 26-33, 35, 37-59, 68-75 is/are rejected.

☒ Claim(s) 34, 36 is/are objected to.

☒ Claim(s) 19, 26-79 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 11

☐ Interview Summary, PTO-413

☐ Notice of References Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Action Summary

Part III: Detailed Office Action

Applicants point out in paper number 14, filed 8/16/02, that the pending claims were misnumbered. Accordingly, claims 68-81 have been renumbered as 66-79. See 37 C.F.R. § 1.126.

Claims 26-79 are under consideration.

The rejection of claims 50-59 and 74-77 under 35 U.S.C. 112, first paragraph, as requiring deposit of organisms under accession number ATCC 97342 is withdrawn in view of applicants' statements filed 8/16/02.

The rejection of claims 32, 33-39, 49, 50-59, 63, 69, 73, and 77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of applicants' amendments.

The rejection of claims 33, 35, 37-39, 50, 52, 55, and 57-59 under 35 U.S.C. 112, first paragraph because the specification fails to adequately describe what is meant by "mature" TGF α HIII is withdrawn in view of applicants' amendments.

The rejection of claims 60-77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Genbank Accession number HO2975 is withdrawn in view of applicants' submission of the Wei declaration.

Formal Matters:

Items AO and AR-AV cited on the information disclosure statement submitted 3/14/02, paper number 11, have been considered. However, the mere provision of a nucleic acid or protein sequence without either an alignment to the disclosed material or explanation of relevance cannot be evaluated for relevancy to the claimed subject matter.

The rejection of claims 26-77 under 35 U.S.C. 101 is withdrawn in view of applicants' argument that the specification asserts that supernatant containing the protein stimulates growth of aortic smooth muscle cells.

Rejections under 35 U.S.C. §112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 40-59, 68-75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the protein of SEQ ID NO: 2 or as encoded by ATCC 97342 or fragments thereof that have the activity of stimulating the growth of aortic smooth muscle cells, does not reasonably provide enablement for proteins 90% or 95% identical to such, nor with protein fragments that have the activity of "regulating cell growth". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. It is noted that this is not a new ground of rejection per se, but rather a narrowing of the total lack of enablement as set forth in the previous Office Action.

As set forth in the previous Office Action, the specification merely discloses the nucleic acid of SEQ ID NO: 1, which is stated to encode SEQ ID NO: 2; no specific variants are disclosed, nor is there guidance as to how to make variants which retain biological activity, nor how to use variants which do not retain such activity. While the specification presents a very extensive prophetic disclosure of numerous conservative and non-conservative substitutions that can be made at each individual position of SEQ ID NO: 2, such is not considered to be specific guidance as to possible variants that may be made with a reasonable expectation of success, because such is merely a listing of thousands of possible changes that *could* be made, with no logic or reason to expect that the function of the resultant molecule would be conserved.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). In this case, although proteins that bind and activate EGF receptors were known in the art, and the relative skill in the art of molecular biology is high, the predictability in the art of altering proteins and retaining function is relatively low, especially where, as in this case, the members of the protein family which bind EGF receptors have a low degree of conservation of amino acid sequences. In this case, the similarity to TGFa shown in Figure 2 is very low, and it has not been established that TGFαH3 binds to the common receptor, the EGF receptor. Taken with the lack of working examples, the lack of *specific* direction or guidance as to alterations which could be made, the breadth of the claims, which in their current state read on a very large scope of proteins, the specification fails to provide enablement commensurate in scope with the claims.

With respect to the scope of fragments that 'regulate cell proliferation', enablement is presented only of stimulation of growth of aortic smooth muscle cells. No other type of cell has been shown to be affected by the presence of the protein of SEQ ID NO: 2, nor is it predictable what other cell types would be similarly affected, nor is there any other showing that would be commensurate in scope with a claim to a protein that "regulates cell proliferation" as in claim 70, which encompasses both positive and negative regulation of any type. The specification merely presents a single working example of an activity, the ability to stimulate aortic smooth muscle cells, and goes on to claim any possible fragment or variant that 'regulates cell proliferation' of any cell, in any fashion. Such is merely an invitation to experiment to determine what other functions the protein may have, and how to use it for such functions.

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentec, Inc, v. Novo*

Nordisk, 42 USPQ 2d 100,(CAFC 1997), the court held that:

> "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one cannot, following the guidance presented therein, practice the suggested method without first making a substantial inventive contribution.

Claims 26-32 and 40-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

It is noted that amendment B, filed 8/16/02 changed the numbering of SEQ ID NO: 2, whereas amendment C, filed 11/8/02, has reverted the numbering to the original. Accordingly, the amendment to the claims (amendment B, paper number 14) introduces new matter, as fragments of 1-204 and 1-177 of SEQ ID NO: 2 as currently numbered are not disclosed in the specification as originally filed.

Advisory Information:

33-39 Claims 60-67 and 76-79 are allowed.

Claims 34 and 36 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703)308-4623.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Spector via telephone number 703-746-5228. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Lorraine Spector

Lorraine Spector, Ph.D.
Primary Examiner

LMS
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1/23/03